REMARKS

The Claims

Claims 1-7 and 10 are currently pending in this application. Claims 6-7 are withdrawn and claims 8-9 are cancelled. Claims 1 and 5 have been amended. No new matter is being hereby introduced. Applicants reserve the right to file a divisional or continuation application directed to the subject matter that has been withdrawn or cancelled herefrom.

Claim 1 has been amended to include the proviso that the antagonist is not native prostaglandin F2 receptor. Support for this amendment may be found throughout the instant specification, for example at page 2, ln. 32 through page 3 ln. 13 of the Background section, which describes the known human FP receptor or prostaglandin F2 receptor (page 1, lns. 31-34). Claim 1 has been further amended by replacing the phrase "containing essentially of" with the term "comprising." Support for the "comprising" language may be found in the original claim as filed.

Claim 5 has been amended for clarity by replacing the term "containing" with "comprising." Although the Examiner suggested improving the syntax of claim 5 by adding the phrase "or a" before the term "mixture," applicants have instead deleted the phrase "mixture thereof, in association with." By reciting "at least one," amended claim 5 continues to cover mixtures of antagonists and therefore retains the scope of the claim prior to amendment.

Applicants respectfully submit that these amendments do not constitute new matter and respectfully request entry thereof.

Claim Rejections under 35 USC § 112, first paragraph – New Matter

Claims 3, 4 and 10 stand rejected under 35 U.S.C. 112, first paragraph, because the Examiner contends that the specification, while being enabling for a method of inhibiting contractions of bovine and porcine uterine muscle *in vitro*, does not reasonably provide enablement for a method of inhibiting uterine contractions in humans, or for inhibiting dysmenorrhea or premature delivery of a fetus. It is the Examiner's position

that the specification does not enable any person skilled in the art to use the invention commensurate in scope with these claims. As it stands, according to the Examiner, the *in vitro* assays are not predictive to the artisan that the prostaglandin receptor antagonists would be effective *in vivo*.

Applicants traverse this objection. Applicants respectfully submit that at the time of filing of the instant application, the role of prostaglandins in pregnancy- related labor was well-documented and had been shown to be indiscriminate of species, *i.e.* the role of these molecules in humans and other mammals is identical (see, for example, Novy MJ and Liggins GC, 1980, Semin. Perinatol., Vol. 4, at page 57, right column, "Initiation of Parturition"). With respect to PGF2α in particular, the ability of this prostaglandin to induce myometrial contractions through the FP receptor had been demonstrated in both humans (Senior, J *et al.*, 1993, J. Pharmacol., 108 at page 501; Fig. 3; Table 1) and other animal species (Novy MJ and Liggins GC, *supra* at page 46, last full paragraph in right column). Accordingly, Applicants assert that a person skilled in the art would consider a demonstration of the ability of a compound, such as the antagonists of the instant invention, to inhibit contractions of bovine, porcine and ovine uterine myometrial strips to be predictive of the ability of these compounds to exert the same effect in a human model. The results from the bovine, porcine, and ovine uterine myometrial strips are indicative of those in a human. Thus, the myometrial strips experiment is an art-accepted animal model for human *in vivo* studies, and one skilled in the art would understand that methods of inhibiting contractions of bovine and porcine uterine muscle *in vitro* provides sufficient enablement for a method of inhibiting uterine contractions in humans or for inhibiting dysmenorrhea or premature delivery of a fetus.

Moreover, as indicated in the Applicants' previous correspondence of August 20, 2003, PCP-13 (also referred to as THG113) has been shown to prolong gestation in a mouse model of preterm labor (Peri, KG *et al.*, 2002, Sem. Perinatol. 26(6): 389-397). Identical animal models have been used to test compounds that have gone on to clinical trials. One such example uses indomethacin (a prostaglandin synthase inhibitor), which was shown to inhibit uterine contractions in animal uterine strips (Yousif MH *et al.*, 1998, J. Pharm. Pharmacol. 50(681-685); see Figures and Discussion section) and to

delay bacterial lipopolysaccharide induced preterm delivery in mice (Lee PR *et al.*, 2003. Am J Obstet Gynecol. 189(1):261-266; see abstract). Several clinical trials have also demonstrated that indomethacin is a good tocolytic in human patients (Morales WJ *et al.*, 1989, Obstet and Gynecol. 74(4) 567-572; see Table 2). Applicants, therefore, respectfully submit that the ability of a compound to inhibit contractions of uterine myometrial strips *in vitro* would be understood and viewed by the skilled artisan as predictive of the ability of the compound to be effective *in vivo*.

Finally, as was previously discussed in the Applicants' correspondence of August 20, 2003, there is a strong correlation between uterine contractions and successful prevention of premature delivery of a fetus *in vivo* or prevention of dysmenorrhea. Applicants assert that the it is commonly known in the art that prostaglandins play a role in myometrial contractions and labor (see, instant application-pg. 1). In addition, Applicants respectfully direct the Examiner's attention to the numerous publications reporting the correlation between uterine myotonic (spastic) activity and pain (for example, Novy MJ and Liggins GC, *supra* at page 61-see *Inhibitors of Prostaglandin Synthesis*; Pulkkinen MO, 1987, J Clin Pharmacol., (27)65-69- see Fig. 4; and Lumsden MA *et al*, 1983, Prostaglandins 25(5): 683-92-par. bridging pgs.689-690) and demonstrating the ability of tocolytics to delay preterm labor (for example, Morales WJ, *supra*; and Gyetvai K *et al.*, 1999, ObGYN 94(5) 869-877-see abstract). Applicants respectfully note that animal data are acceptable to show efficacy for enablement purposes in an application, see MPEP § 2164.02. In *In re Scott v. Finney*, 34 F.3d 1058 (Fed. Cir. 1994) and *In re Cross v. Iizuka*, 753 F.2d 1040 (Fed. Cir. 1985), the Federal Circuit held that animal testing was sufficient for showing a reduction to practice for human applications.

Based on the above discussion, Applicants submit that the *in vitro* tests described in the instant application are indicative of successful treatment of the methods of claims 3, 4 and 10 *in vivo*. Accordingly, one skilled in the art having regard to the present specification would be able to practice the instant invention without undue experimentation in view of the art and the specification of the instant application. Applicants assert that the breadth of the above-referenced claims are not excessive and

respectfully request that the Examiner reconsider and withdraw this 35 U.S.C. §112, first paragraph rejection.

Claim Rejections under 35 USC § 102

Claims 1 and 5 stand rejected under 35 U.S.C. 102(b) as being anticipated by Abramovitz *et al.* (WO 95/00551). The Examiner alleges that the Abramovitz *et al.* publication describes a PGF2 receptor comprising at least SEQ ID NO:1 of the present invention and that the full length PGF2 receptor would act as an antagonist to the endogenous PGF2 receptor. Although the antagonist of the instant claim 1 consists essentially of SEQ ID NO:1, the Examiner alleges that the use of the phrase 'consisting essentially of' still allows for reading on the full length receptor.

The Examiner further states that Abramovitz *et al.* reports of a pharmaceutical composition as exemplified by the buffers used in the PGF2 binding assays (Experiment 7). As such, the Examiner contends that a person skilled in the art would immediately envision the protein in a pharmaceutical composition such as a buffer or water.

Applicants respectfully traverse this rejection. Applicants respectfully direct the Examiner's attention to M.P.E.P. §2111.03, which relates to the interpretation of transitional phrases. According to §2111.03, use of the phrase 'consisting essentially of' limits the scope of the claim to the specified materials or steps and those that do not materially affect the basic and novel characteristic(s) of the claimed invention. With respect to the instant invention, one of the basic and novel characteristic of claim 1 is an antagonist of the PGF2 receptor consisting essentially of SEQ ID NO:1. Although the Examiner alleges that the full-length PGF2 receptor disclosed by Abramovitz *et al.*, which includes SEQ ID NO:1, may also act as an antagonist to the endogenous PGF2 receptor by binding excess agonist in the body, Applicants respectfully disagree. It is well known in the art that membrane proteins (such as receptors), when taken out of the membrane environment, are unable to adopt their active tertiary structure. It would be highly unlikely, therefore, that the PGF2 receptor disclosed by Abramovitz *et al.*, if administered to a subject, would be able to bind the PGF2 agonist and thereby function as an antagonist of the endogenous PGF2 receptor. Accordingly, a person skilled in the art

would not expect the antagonist of Claim 1 to include the PGF2 receptor, which is 359 amino acids in length, as disclosed by Abramovitz *et al.*

The Applicants also respectfully submit that in order to anticipate a claim, the reference must teach every element of the claim (see MPEP 2103).

> "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). "The identical invention must be shown in as complete detail as is contained in the ... claim." *Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989).

Amended Claim 1 of the instant application is directed towards a prostaglandin F2 receptor antagonist comprising specific sequences, one of which is SEQ ID NO:1. Although the Examiner alleges that the full-length PGF2 receptor disclosed by Abramovitz *et al.* may be used as an antagonist, the cited prior art fails to disclose the use of SEQ ID NO:1 or the PGF2 receptor as an antagonist. Furthermore, as discussed above, the receptor as disclosed by Abramovitz *et* al. would not function as an antagonist.

In order to expedite prosecution of this application, Applicants have amended Claim 1 to clarify that the instant claim is not directed towards the native prostaglandin F2 receptor, which is discussed in the Background section of the instant application. Amending the claim to replace "consisting essentially of" with "comprising" does not introduce new matter since the claim as originally filed utilized the term "comprising." Thus, for the above-mentioned reasons, applicants respectfully submit that claims 1 and 5 are not anticipated by Abramovitz *et al.* Based on the previous arguments and what is commonly known and understood in the art, reconsideration and withdrawal of this 35 U.S.C. §102 rejection is respectfully requested.

AUTHORIZATION

No additional fees are believed to be necessitated by this amendment. However, should this be an error, authorization is hereby given to charge Deposit Account No. 13-4500, Order No. 4591-4000 for any underpayment or to credit any overpayment.

Respectfully submitted,
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